REMARKS

Claims 4, 7, 10-11, 14, 17-22, 26-31, and 41 are pending in this application. Claims 29-30 have been canceled and new claims 43-64 have been added. Claims 28, 31, and 41 have been amended. Support for the amendments can be found throughout the specification and original claims, for example, in original claims 4, 7, 10-11, 14, and 17-22 (particular species); Table A at pages 29-32 (particular species); page 4, lines 28-30 (method of producing a pharmaceutical composition); page 3, lines 27-30, page 4, lines 19-22, and page 10, lines 14-17 (methods of treating dylipidemia, e.g., by lowering triglycerides or free fatty acids in an individual). No new matter has been added. After entry of this amendment, claims 4, 7, 10-11, 14, 17-22, 26-28, 31, 41, and 43-64 will be pending in this application.

As a preliminary matter, Applicants thank the Examiner for the withdrawal of the restriction requirement as indicated on page 2 of the Office Action.

I. Information Disclosure Statement

Enclosed is a supplemental information disclosure statement for consideration by the Examiner. Applicants thank the Examiner for her consideration of the previously submitted IDS.

II. The Claims Are Enabled

A. Methods of Treatment

Claims 28-31 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the enablement requirement. The Office alleges that the specification does not reasonably provide enablement for methods of treating all types of metabolic-related disorders, dyslipidemia, coronary heart disease, and insulin resistance or a method of raising HDL.

As a preliminary matter, Applicants wish to clarify the record with regard to statements in the Office Action. The Office states that the instant compounds were tested in *in vivo* tests and animal models (Office Action, page 6). Applicants respectfully note for the record that Example 1, 2, and 5 are prophetic in nature. Applicants direct the Office's attention to the use of the present tense throughout these examples.

Further, in delineating the alleged state of the prior art, the Office has cited Sparatore, et al., *Chem. & Biodiver.*, 3:385-395 (2006) ("Sparatore") and Semple, et al., *J. Med. Chem.*, 49:1227-1230 (2006) ("Semple"). Applicants note that Sparatore and Semple were published in 2006, after the filing date of October 29, 2004 of PCT/US2004/035927, of which the present application is a § 371 National Stage application. Hence, Sparatore and Semple do not form part of the "state of the prior art".

Applicants respectfully assert that the claims 28 and 31, and dependent claims thereof, meet all of the requirements of 35 U.S.C. § 112, first paragraph. In order to advance prosecution, Applicants have canceled claims 29 and 30 and amended claims 28 and 31 to recite a method of lowering triglycerides in an individual and a method of lowering free fatty acids individual, respectively, comprising the administration of particular species of Formula (I). Applicants further added dependent claims 43-64. The amended claims meet the enablement requirement, because: (1) nicotinic acid (niacin) was known at the time of filing to have activity in lowering triglycerides and free fatty acids as recited by claims 28 and 31; (2) the murine variant of the known RUP25 receptor was shown to mediate the metabolic effects of nicotinic acid; (3) nicotinic acid was known to bind to and agonize the RUP25 receptor; and (4) the particular species of Formula (I) recited by the claimed methods also bind to and agonize the RUP25 receptor. As a result, one of skill in the art would recognize that an agonist of the RUP25 receptor, such as the compounds of claims 28 and 31, and dependent claims thereof, would be expected to have efficacy in lowering triglycerides and free fatty acids as does nicotinic acid. Accordingly, Applicants assert one of skill in the art could have practiced the claimed methods at the time the present application was filed without undue experimentation.

As will be recognized, the enablement requirement of §112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the

following statement from *In re Marzocchi*, 169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971), is noteworthy:

> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.
>
> ... it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

Thus, any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974). Further, the proper standard for an enablement inquiry rests on whether one skilled in the art would be able to make and use the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q.2d at 1404. Factors for consideration in determining whether undue experimentation is necessary to make and use the invention include 1) the quantity of experimentation necessary; 2) the amount of direction or guidance presented; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims.

Applicants respectfully assert that the Office has not carried its burden to provide evidence showing a sufficient reason to doubt the enablement of claims 28 and 31, or dependent claims thereof, in light of the guidance provided by the specification and the state of the art regarding the RUP25 receptor and nicotinic acid. As stated in the specification, nicotinic acid

(niacin) was known prior to filing to have efficacy in lowering triglycerides and free fatty acids. For example, administration of 1 g. of niacin three times daily decreased triglycerides by 26% in individuals in one study. *See* Guyton, "Effect of Niacin on Atherosclerotic Cardiovascular Disease", *Am. J. Cardiol.* 82(12A):18U-23U, at page 18U (1998) (hereinafter "Guyton", enclosed for the Examiner's convenience); *see also*, Tunaru, et al., "PUMA-G and HM74 are receptors for nicotinic acid and mediate its anti-lipolytic effect", *Nature Medicine*, 9(3):352-355, at 354 (March 2003) (hereinafter "Tunaru", enclosed for the Examiner's convenience, showing reduction in triglyceride levels for wild-type mice). Further, nicotinic acid was known to reduce the level of free fatty acids in wild-type mice. *See* Tunaru at 353-54. Hence, Guyton and Tunaru demonstrates that there was ample evidence of the efficacy of nicotinic acid for lowering triglycerides and free fatty acids.

Further, nicotinic acid was known prior to filing to bind to a particular receptor – RUP25 – also known as the HM74A receptor or the GPR109A receptor (see GeneBank record for GeneBank Accession No. NM_177551 for the nucleotide and GeneBank Accession No. NP_808219 for the polypeptide referenced at page 50, lines 1-6 of the specification; see also, Wise, et al. "Molecular Identification of the High and Low Affinity Receptors for Nicotinic Acid", *J. Biolog. Chem.*, 278(11):9869-9874 (2003), enclosed for the Examiner's convenience). The murine homologue of HM74A – RUP25 – is known as PUMA-G. Studies conducted before the date of filing were consistent with PUMA-G mediating the main metabolic effects of nicotinic acid, including lowering free fatty acid and triglyceride levels. *See* Tunaru at 353-354. Hence, there is ample pre-filing evidence tying the RUP25 receptor to the efficacy of nicotinic acid in lowering triglycerides and free fatty acids such as in the claimed methods.

Further, nicotinic acid was known to function as an agonist at the RUP25 receptor. *See* Wise at 9872. Hence, other agonists of the RUP25 receptor should have efficacy in treating the same disorders treatable by nicotinic acid. As asserted in the specification, the species recited by the methods of claims 28 and 31, and dependent claims thereof, bind to and agonize the RUP25 receptor and, therefore, would be expected to have efficacy in lowering triglycerides and free fatty acids as does nicotinic acid.

Hence, at the time of filing, (1) nicotinic acid was known to have activity in lowering triglycerides and free fatty acids as recited by the claims; (2) the murine variant of the known RUP25 receptor was shown to mediate the metabolic effects of nicotinic acid; (3) nicotinic acid was known to bind to and agonize the RUP25 receptor; and (4) the novel claimed compounds of Formula (I) also bind to and agonize the RUP25 receptor. As a result, one of skill in the art would recognize that an agonist of the RUP25 receptor, such as the compounds recited by the methods of claims 28 and 31, would be expected to have efficacy in lowering triglycerides and free fatty acids as does nicotinic acid. Accordingly, in light of the working examples described above, the guidance provided by the specification, and the state of the art regarding the RUP25 receptor and nicotinic acid, Applicants assert one of skill in the art could have practiced the claimed methods at the time the present application was filed without undue experimentation. The Office has failed to point to any evidence to doubt the objective truth of the statements contained by the specification as required by in *In re Marzocchi*. Applicants, therefore, respectfully request that all of the requirements of 35 U.S.C. § 112, first paragraph, have been met and request that the claim rejections be withdrawn.

B. Solvates and Hydrates

Claims 4, 7, 10, 11, 14, 17-22, 26-28, 31, and 41 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement with regard to the solvates and hydrates of the claimed compounds. The Office alleges that the specification "does not reasonably provide enablement for solvates or hydrates of [the claimed] compounds" (Office Action, page 7). Citing to *Morton International Inc. v. Cardinal Chemical Co.*, 28 U.S.P.Q.2d 1190 (Fed. Cir. 1993), the Offices states that that "[t]here is no evidence that solvates or hydrates of the instantly claimed compounds exist" because [i]f they did, they would have been formed" (Office Action, page 8). Because there are allegedly an "extremely large number of solvates and hydrates...could be encompassed by the claims", the Office states that "nothing short of extensive testing (none identified) would be needed to determine if additional derivatives exist and thus, such as scope as literally claimed herein is non-enabled" (Office Action, page 10). The

Office has further stated that "[i]t is not the norm that one can predict with any accuracy a particular solvate form of an active compound will be more soluble, more easily handled in formulations or more bioavailable without actual testing *in vivo*" (Office Action, page 8).

As a preliminary matter, the Office's reliance on *Morton* is misplaced. In *Morton*, the claims were directed to organotin compounds having "partial connectivity". *Morton*, 28 U.S.P.Q.2d at 1193. Noting that both the defendant and patentee had both expended "[e]ven with the aid of sophisticated analytical instrumentation and the use of model systems", there was no evidence that the claimed compounds with the required connectivity could even exist. *Id.* Further, there was no evidence the procedures in the specification or the defendant's process would produce compounds with the "partial connectivity". *Id.* at 1193-94. Applicants respectfully assert that the claimed solvates and hydrates present a far different situation from that in *Morton*. As summarized below, there is clear evidence that hydrates and solvates are quite common and can be formed by routine methods. Hence, there is no question that hydrates and solvates can exist, unlike the compounds having partial connectivity in *Morton*. Further, unlike the failed preparative routes in *Morton*, the Office has failed to point to any section of the specification which suggests that Applicants attempted and failed to produce a solvate or hydrate of the claimed compounds.

As to the Office's statement that "[i]t is not the norm that one can predict with any accuracy a particular solvate form of an active compound will be more soluble, more easily handled in formulations or more bioavailable without actual testing *in vivo*" (Office Action, page 8), Applicants respectfully note that compliance with § 112, first paragraph, does not require that the solvates or hydrates be **more** bioavailable or **more** easily handled than the compounds of Formula I. Rather, it is sufficient to show that the solvates and hydrates can be made and used without undue experimentation.

Moreover, Applicants respectfully assert that the Office has not carried its burden to provide evidence or reasoning showing a sufficient reason to doubt that one of skill in the art could make the hydrates and solvates of the claimed compounds without undue experimentation. As will be appreciated, the test for whether experimentation would be undue is not merely

quantitative since a considerable amount of experimentation is permissible, if it is merely routine. *Wands*, 8 U.S.P.Q.2d at 1404. In *Wands*, the Office had rejected the appealed claims, directed to methods for assaying HBsAg using high-affinity IgM monoclonal antibodies, as lacking enablement. *Id.* at 1402. The Office alleged that the production of high-affinity IgM anti-HBsAg antibodies was unpredictable and unreliable and, therefore, would require undue experimentation. *Id.* The Federal Circuit disagreed, finding that undue experimentation would not be required. *Id.* at 1406. Even though screening for hybridomas involved several, labor-intensive steps (see the steps in Table 1), the court found that this amount of effort was not excessive or undue, as the methods needed to practice the invention were well-known and the level of skill in the art was high. *Id.* The court noted that a finding of undue experimentation would not be required even if the success rate for producing the antibodies was only 2.8% as suggested by the Office (as contrasted with the 44% success rate advanced by the applicant). *Id.*

In stark contrast with the antibody-making procedures at issue in *Wands*, the preparation of hydrates and solvates of a particular organic molecule is a substantially easier and overwhelmingly simpler process, which requires significantly fewer steps and much less time than the preparation of a monoclonal antibody. Table 1 provides a step-by-step comparison of some of the major steps involved in the production of a monoclonal antibody (as disclosed in *Wands*) and the one step involved in making a hydrate or solvate. To make hydrates and solvates, samples of the organic compound are exposed to water or various different solvents.[1]

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[1] For example, Guillory, "Generation of Polymorphs, Hydrates, Solvates, and Amorphous Solids", in Polymorphism in Pharmaceutical Solids, ed. Harry G. Brittain, vol. 95, chapter 5, Marcel Dekker, Inc., New York 1999, pages 183-226 (hereinafter "Guillory") at pages 202-205 and pages 205-208 describe the routine preparation of hydrates and solvates of compounds, respectively, as illustrated in the excerpts below:

> Simply exposing an anhydrous powder to high relative humidity can often lead to formation of a hydrate.

Guillory, page 204.

> Often, when solvents are employed in the purification of new drug substances by recrystallization, it is observed that the isolated crystals include solvent molecules...

Guillory, page 205.

Once the hydrates and solvates are formed, they can be readily analyzed by routine methods or other routine techniques to detect and quantify the presence of hydrate or solvate molecules in the sample. Exposure of the organic compounds to water and various solvents is conducted through simple and routine methods such as letting the samples sit open to air for set amounts of time, as well as slurrying and/or crystallizing the samples from water or solvent. In fact, it is difficult to conceive of a scientific method that is simpler to perform than placing a powder on a dish and letting it sit out on a humid day. Other typical procedures for making and identifying hydrates and solvates are described in Guillory, "Generation of Polymorphs, Hydrates, Solvates, and Amorphous Solids", in Polymorphism in Pharmaceutical Solids, ed. Harry G. Brittain, vol. 95, chapter 5, Marcel Dekker, Inc., New York 1999, pages 183-226 (hereinafter "Guillory") (enclosed). Hence, screening for hydrates and solvates merely uses methods that are very well known in the art and considered quite simple.[2] As is clearly shown in Table 1 and summarized above, the production of a monoclonal antibody is much more complex and time-consuming than the production of a hydrate or solvate, yet the *Wands* court concluded that the production of a monoclonal antibody was not excessive and undue. Hence, it is clearly inconsistent to allege that the production of hydrates and solvates would require undue experimentation, while the production of monoclonal antibodies would not require undue experimentation.

The Office attempts to base its enablement rejection on unpredictability of solvate formation and (2) lack of working examples. Unpredictability was a major reason for the Office's rejection of the claims in *Wands*, yet the rejection was reversed by the Federal Circuit because, in part, all the methods needed to practice the invention were well-known and the level in the art was high. Accordingly, any unpredictability associated with hydrate or solvate formation that might exist is clearly outweighed by the fact that preparing and screening for hydrates and solvates is routine and employs well-known methods. With respect to lack of working examples, the courts have held that there is no requirement for a "working" example if the disclosure is such that one skilled in the art can practice the claimed invention. *In re*

[2] In fact, there are numerous companies that routinely provide this screening service (usually combined with polymorph screens) and advertise how quickly and efficiently they can identify hydrates and solvates. Example companies offering these services include Wilmington PharmaTech (Wilmington, DE) and Avantium Technologies (Amsterdam).

Borkowski, 164 U.S.P.Q. 642 (C.C.P.A. 1970); *Ex parte Nardi*, 229 U.S.P.Q. 79 (Pat. Off. Bd. App. 1986). Given that one skilled in the art could make and identify various hydrates and solvates of a particular organic molecule using the routine screening methods discussed above, no working example is necessary to enable the invention.

Further, after searching the PTO database of issued patents in a cursory manner, the following U.S. Patents were readily identified as having claims including hydrates and/or solvates, yet having no enablement rejections to the same: U.S. Pat. Nos. 7232823, 7230024, 7229991, 7211591, 7173037, 7157466, and 7105523. Applicants see no difference between these patents and the present application with respect to enablement of hydrates and solvates and, thus, believe that the enablement rejection in this application should be withdrawn. For all of these reasons, Applicants respectfully assert that all of the requirements of 35 U.S.C. § 112, first paragraph, have been met and request that the claim rejections be withdrawn.

Table 1

Step	Monoclonal Antibody	Hydrate or Solvate
1	immunize animal	expose the compound to water or solvent
2	remove the spleen from the immunized animal	
3	separate the lymphocytes from the other spleen cells	
4	mix the lymphocytes with myeloma cells	
5	treat the mixture to cause fusion between the lymphocytes and the myeloma cells to make hybridomas that hopefully secrete the desired antibody	
6	separate the hybridoma cells from the unfused lymphocytes and myeloma cells by culturing in a medium in which only hybridoma cells survive	

Step	Monoclonal Antibody	Hydrate or Solvate
7	culture single hybridoma cells (often 100 of different cells) in separate chambers	
8	assay the antibody secreted from each hybridoma culture to determine if it binds to the antigen	

III. The Claims Are Definite

Claim 41 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Office alleges that the claim is indefinite for omitting the reagents and an "active, positive step" (Office Action, page 11). Claim 41 has been amended to recite that the step of "admixing a compound according to claim 4, or a pharmaceutically acceptable salt, solvate or hydrate thereof, *with a pharmaceutically acceptable carrier*" (emphasis added).[3] Applicants respectfully that claim 41 now recites the active step of "admixing" a compound of claim 4 with a reagent — the pharmaceutically acceptable carrier. Applicants, therefore, respectfully assert that all of the requirements of 35 U.S.C. § 112, second paragraph, have been met and request that the claim rejection be withdrawn.

IV. Provisional Obviousness-type Double Patenting

Claims 28-31 and 41 are provisionally rejected over claims 28-31 and 41-43 of Patent Appl. No. 11/601,252 ("'252 application") under the judicially-created doctrine of obviousness-type double patenting. While Applicants note that the present application is senior to the '252 application and should be allowed to issue if the present application is found to be allowable, Applicants have expressly abandoned the '252 by a petition under 37 C.F.R. § 1.138 submitted on this same date. Accordingly, Applicants respectfully request that the rejection be withdrawn.

[3] Applicants note that the italicized phrase appears to have been inadvertently deleted in the last amendment to the claims. Accordingly, the current amendment merely returns claim 41 to its original form and, therefore, does not narrow the claim or add any new matter.

V. Conclusion

Applicants respectfully assert that rejections of record have been overcome by way of this response. Allowance of all claims is respectfully requested. The Examiner is urged to contact Applicant's undersigned representative at (302) 778-8411 if there are any questions regarding the claimed invention. Applicants reserve the right to pursue the subject matter of canceled or amended subject matter in one or more continuing applications.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to Deposit Account No. 06-1050. Further, if not accompanied by an independent petition, this paper constitutes a Petition for an Extension of Time for an amount of time sufficient to extend the deadline if necessary and authorizes the Commissioner to debit the petition fee and any other fees or credit any overpayment to Deposit Account No. 06-1050.

Respectfully submitted,

Date: December 17, 2008

Susanne H. Goodson
Reg. No. 58,450

Fish & Richardson P.C.
P.O. Box 1022
Minneapolis, MN 55440-1022
Telephone: (302) 652-5070
Facsimile: (877) 769-7945

Enclosed: Information Disclosure Statement
GeneBank record for GeneBank Records for Accession No. NM_177551 and Accession No. NP_808219

1: NP_808219. Reports G protein-coupled...[gi:29171311]

BLink, Conserved Domains, Links

Comment Features Sequence

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VERSION     NP_808219.1  GI:29171311
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REFERENCE   1  (residues 1 to 363)
  AUTHORS   Knouff,C.W., Lim,N., Song,K., Yuan,X., Walker,M.C., Townsend,R.,
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            Mooser,V.
  TITLE     Pharmacological effects of lipid-lowering drugs recapitulate with a
            larger amplitude the phenotypic effects of common variants within
            their target genes
  JOURNAL   Pharmacogenet. Genomics (2008) In press
   PUBMED   18787507
  REMARK    GeneRIF: Observational study of gene-disease association. (HuGE
            Navigator)
            Publication Status: Available-Online prior to print
REFERENCE   2  (residues 1 to 363)
  AUTHORS   Miller,C.L. and Dulay,J.R.
  TITLE     The high-affinity niacin receptor HM74A is decreased in the
            anterior cingulate cortex of individuals with schizophrenia
  JOURNAL   Brain Res. Bull. 77 (1), 33-41 (2008)
   PUBMED   18639743
  REMARK    GeneRIF: Data show that the high-affinity niacin receptor HM74A is
            significantly down-regulated in the anterior cingulate cortex of
            individuals with schizophrenia.
REFERENCE   3  (residues 1 to 363)
  AUTHORS   Kostylina,G., Simon,D., Fey,M.F., Yousefi,S. and Simon,H.U.
  TITLE     Neutrophil apoptosis mediated by nicotinic acid receptors (GPR109A)
  JOURNAL   Cell Death Differ. 15 (1), 134-142 (2008)
   PUBMED   17932499
  REMARK    GeneRIF: neutrophils express functional GPR109A receptors,which
            might be involved in the regulation of neutrophil numbers
REFERENCE   4  (residues 1 to 363)
  AUTHORS   Tang,Y., Zhou,L., Gunnet,J.W., Wines,P.G., Cryan,E.V. and
            Demarest,K.T.
  TITLE     Enhancement of arachidonic acid signaling pathway by nicotinic acid
            receptor HM74A
  JOURNAL   Biochem. Biophys. Res. Commun. 345 (1), 29-37 (2006)
   PUBMED   16674924
  REMARK    GeneRIF: However, the synergistic effects of HM74A were not
            dramatically affected by co-treatment with both inhibitors,
            indicating the cross-talk occurred at the receptor level.
REFERENCE   5  (residues 1 to 363)
  AUTHORS   Zhang,Y., Schmidt,R.J., Foxworthy,P., Emkey,R., Oler,J.K.,
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Large,T.H., Wang,H., Su,E.W., Mosior,M.K., Bacho,P.I. and Cao,G.
TITLE Niacin mediates lipolysis in adipose tissue through its G-protein coupled receptor HM74A
JOURNAL Biochem. Biophys. Res. Commun. 334 (2), 729-732 (2005)
PUBMED 16018973
REMARK GeneRIF: Our results provided direct evidence indicating that HM74A, but not HM74, was sufficient to mediate anti-lipolytic effect of niacin in adipose tissue.
REFERENCE 6 (residues 1 to 363)
AUTHORS Soga,T., Kamohara,M., Takasaki,J., Matsumoto,S., Saito,T., Ohishi,T., Hiyama,H., Matsuo,A., Matsushime,H. and Furuichi,K.
TITLE Molecular identification of nicotinic acid receptor
JOURNAL Biochem. Biophys. Res. Commun. 303 (1), 364-369 (2003)
PUBMED 12646212
REMARK GeneRIF: HM74b has high similarity to HM74 is a receptor for nicotinic acid [HM74b]
REFERENCE 7 (residues 1 to 363)
AUTHORS Wise,A., Foord,S.M., Fraser,N.J., Barnes,A.A., Elshourbagy,N., Eilert,M., Ignar,D.M., Murdock,P.R., Steplewski,K., Green,A., Brown,A.J., Dowell,S.J., Szekeres,P.G., Hassall,D.G., Marshall,F.H., Wilson,S. and Pike,N.B.
TITLE Molecular identification of high and low affinity receptors for nicotinic acid
JOURNAL J. Biol. Chem. 278 (11), 9869-9874 (2003)
PUBMED 12522134
REFERENCE 8 (residues 1 to 363)
AUTHORS Takeda,S., Kadowaki,S., Haga,T., Takaesu,H. and Mitaku,S.
TITLE Identification of G protein-coupled receptor genes from the human genome sequence
JOURNAL FEBS Lett. 520 (1-3), 97-101 (2002)
PUBMED 12044878
REMARK Erratum:[FEBS Lett 2002 Jul 17;523(1-3):257]
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On Dec 17, 2003 this sequence version replaced gi:29744333.
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/db_xref="HPRD:16453"
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Comment Features Sequence

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            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 2082)
  AUTHORS   Kostylina,G., Simon,D., Fey,M.F., Yousefi,S. and Simon,H.U.
  TITLE     Neutrophil apoptosis mediated by nicotinic acid receptors (GPR109A)
  JOURNAL   Cell Death Differ. 15 (1), 134-142 (2008)
   PUBMED   17932499
  REMARK    GeneRIF: neutrophils express functional GPR109A receptors,which
            might be involved in the regulation of neutrophil numbers
REFERENCE   2  (bases 1 to 2082)
  AUTHORS   Tang,Y., Zhou,L., Gunnet,J.W., Wines,P.G., Cryan,E.V. and
            Demarest,K.T.
  TITLE     Enhancement of arachidonic acid signaling pathway by nicotinic acid
            receptor HM74A
  JOURNAL   Biochem. Biophys. Res. Commun. 345 (1), 29-37 (2006)
   PUBMED   16674924
  REMARK    GeneRIF: However, the synergistic effects of HM74A were not
            dramatically affected by co-treatment with both inhibitors,
            indicating the cross-talk occurred at the receptor level.
REFERENCE   3  (bases 1 to 2082)
  AUTHORS   Zhang,Y., Schmidt,R.J., Foxworthy,P., Emkey,R., Oler,J.K.,
            Large,T.H., Wang,H., Su,E.W., Mosior,M.K., Eacho,P.I. and Cao,G.
  TITLE     Niacin mediates lipolysis in adipose tissue through its G-protein
            coupled receptor HM74A
  JOURNAL   Biochem. Biophys. Res. Commun. 334 (2), 729-732 (2005)
   PUBMED   16018973
  REMARK    GeneRIF: Our results provided direct evidence indicating that
            HM74A, but not HM74, was sufficient to mediate anti-lipolytic
            effect of niacin in adipose tissue.
REFERENCE   4  (bases 1 to 2082)
  AUTHORS   Soga,T., Kamohara,M., Takasaki,J., Matsumoto,S., Saito,T.,
            Ohishi,T., Hiyama,H., Matsuo,A., Matsushime,H. and Furuichi,K.
  TITLE     Molecular identification of nicotinic acid receptor
  JOURNAL   Biochem. Biophys. Res. Commun. 303 (1), 364-369 (2003)
   PUBMED   12646212
  REMARK    GeneRIF: HM74b has high similarity to HM74 is a receptor for
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nicotinic acid [HM74b]
REFERENCE 5 (bases 1 to 2082)
AUTHORS Wise,A., Foord,S.M., Fraser,N.J., Barnes,A.A., Elshourbagy,N., Eilert,M., Ignar,D.M., Murdock,P.R., Steplewski,K., Green,A., Brown,A.J., Dowell,S.J., Szekeres,P.G., Hassall,D.G., Marshall,F.H., Wilson,S. and Pike,N.B.
TITLE Molecular identification of high and low affinity receptors for nicotinic acid
JOURNAL J. Biol. Chem. 278 (11), 9869-9874 (2003)
PUBMED 12522134
REFERENCE 6 (bases 1 to 2082)
AUTHORS Takeda,S., Kadowaki,S., Haga,T., Takaesu,H. and Mitaku,S.
TITLE Identification of G protein-coupled receptor genes from the human genome sequence
JOURNAL FEBS Lett. 520 (1-3), 97-101 (2002)
PUBMED 12044878
REMARK Erratum:[FEBS Lett 2002 Jul 17;523(1-3):257]
COMMENT VALIDATED REFSEQ: This record has undergone validation or preliminary review. The reference sequence was derived from AL698846.1, BC027965.1, BC056419.1, AL572062.2 and CD364466.1.
On Jan 23, 2004 this sequence version replaced gi:31343517.

PRIMARY

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1548-2063	BC056419.1	1520-2035	
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